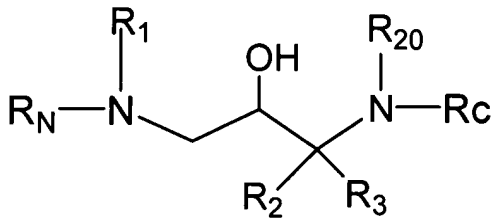
## Listing of Claims

This listing of claims replaces all prior versions and listings of claims in the application.

Claim 1. (original) A compound of the formula I:




or a pharmaceutically acceptable salt or ester thereof, wherein $R_{20}$ is H, $C_{1-6}$ alkyl or alkenyl, $C_{1-6}$ haloalkyl or $C_{4-7}$ cycloalkyl; $R_1$ is $-(CH_2)_{1-2}-S(O)_{0-2}-(C_1-C_6$ alkyl), or

$C_1-C_{10}$ alkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, =O, -SH, $-C\equiv N$, $-CF_3$, $-C_1-C_3$ alkoxy, amino, mono- or dialkylamino, $-N(R)C(O)R'-$, $-OC(=O)-$amino and $-OC(=O)-$mono- or dialkylamino, or

$C_2-C_6$ alkenyl or $C_2-C_6$ alkynyl, each of which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, -SH, $-C\equiv N$, $-CF_3$, $C_1-C_3$ alkoxy, amino, and mono- or dialkylamino, or

aryl, heteroaryl, heterocyclyl, $-C_1-C_6$ alkyl-aryl, $-C_1-C_6$ alkyl-heteroaryl, or $-C_1-C_6$ alkyl-heterocyclyl, where the ring portions of each are optionally substituted with 1, 2, 3, or 4 groups independently selected from halogen, -OH, -SH, $-C\equiv N$, $-NR_{105}R'_{105}$, $-CO_2R$, $-N(R)COR'$, or $-N(R)SO_2R'$, $-C(=O)-(C_1-C_4)$ alkyl, $-SO_2-$amino, $-SO_2-$mono or dialkylamino, $-C(=O)-$amino, $-C(=O)-$mono or dialkylamino, $-SO_2-(C_1-C_4)$ alkyl, or

$C_1-C_6$ alkoxy optionally substituted with 1, 2, or 3 groups which are independently selected from halogen, or

$C_3$-$C_7$ cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, -SH, -C≡N, $-CF_3$, $C_1$-$C_3$ alkoxy, amino, -$C_1$-$C_6$ alkyl and mono- or dialkylamino, or

$C_1$-$C_{10}$ alkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, -SH, -C≡N, $-CF_3$, -$C_1$-$C_3$ alkoxy, amino, mono- or dialkylamino and -$C_1$-$C_3$ alkyl, or

$C_2$-$C_{10}$ alkenyl or $C_2$-$C_{10}$ alkynyl each of which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, -SH, -C≡N, $-CF_3$, $C_1$-$C_3$ alkoxy, amino, $C_1$-$C_6$ alkyl and mono- or dialkylamino; and the heterocyclyl group is optionally further substituted with oxo;

R and R' independently are hydrogen, $C_1$-$C_{10}$ alkyl, $C_1$-$C_{10}$ alkylaryl or $C_1$-$C_{10}$ alkylheteroaryl;

$R_C$ is hydrogen, $-(CR_{245}R_{250})_{0-4}$-aryl, $-(CR_{245}R_{250})_{0-4}$-heteroaryl, $-(CR_{245}R_{250})_{0-4}$-heterocyclyl, $-(CR_{245}R_{250})_{0-4}$-aryl-heteroaryl, $-(CR_{245}R_{250})_{0-4}$-aryl-heterocyclyl, $-(CR_{245}R_{250})_{0-4}$-aryl-aryl, $-(CR_{245}R_{250})_{0-4}$-heteroaryl-aryl, $-(CR_{245}R_{250})_{0-4}$-heteroaryl-heterocyclyl, $-(CR_{245}R_{250})_{0-4}$-heteroaryl-heteroaryl, $-(CR_{245}R_{250})_{0-4}$-heterocyclyl-heteroaryl, $-(CR_{245}R_{250})_{0-4}$-heterocyclyl-heterocyclyl, $-(CR_{245}R_{250})_{0-4}$-heterocyclyl-aryl, $-[C(R_{255})(R_{260})]_{1-3}$-CO-N-$(R_{255})_2$, $-CH(aryl)_2$, $-CH(heteroaryl)_2$, $-CH(heterocyclyl)_2$, -CH(aryl)(heteroaryl), $-(CH_2)_{0-1}$-$CH((CH_2)_{0-6}$-OH)-$(CH_2)_{0-1}$-aryl, $-(CH_2)_{0-1}$-$CH((CH_2)_{0-6}$-OH-$(CH_2)_{0-1}$-heteroaryl, -CH(-aryl or -heteroaryl)-CO-O($C_1$-$C_4$ alkyl), -$CH(-CH_2$-OH)-CH(OH)-phenyl-$NO_2$, ($C_1$-$C_6$ alkyl)-O-($C_1$-$C_6$ alkyl)-OH; $-CH_2$-NH-$CH_2$-$CH(-O-CH_2-CH_3)_2$, $-(CH_2)_{0-6}$-$C(=NR_{235})(NR_{235}R_{240})$, or

$C_1$-$C_{10}$ alkyl optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of

$R_{205}$, $-OC=ONR_{235}R_{240}$, $-S(=O)_{0-2}(C_1-C_6$ alkyl), -SH, $-NR_{235}C=ONR_{235}R_{240}$, $-C=ONR_{235}R_{240}$, and $-S(=O)_2NR_{235}R_{240}$, or

$-(CH_2)_{0-3}-(C_3-C_8)$ cycloalkyl wherein the cycloalkyl is optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of $R_{205}$, $-CO_2H$, and $-CO_2-(C_1-C_4$ alkyl), or

cyclopentyl, cyclohexyl, or cycloheptyl ring fused to aryl, heteroaryl, or heterocyclyl wherein one, two or three carbons of the cyclopentyl, cyclohexyl, or cycloheptyl is optionally replaced with a heteroatom independently selected from NH, $NR_{215}$, O, or $S(=O)_{0-2}$, and wherein the cyclopentyl, cyclohexyl, or cycloheptyl group can be optionally substituted with one or two groups that are independently $R_{205}$, =O, $-CO-NR_{235}R_{240}$, or $-SO_2-(C_1-C_4$ alkyl), or

$C_2-C_{10}$ alkenyl or $C_2-C_{10}$ alkynyl, each of which is optionally substituted with 1, 2, or 3 $R_{205}$ groups, wherein

each aryl and heteroaryl is optionally substituted with 1, 2, or 3 $R_{200}$, and wherein each heterocyclyl is optionally substituted with 1, 2, 3, or 4 $R_{210}$;

$R_{200}$ at each occurrence is independently selected from -OH, $-NO_2$, halogen, $-CO_2H$, C≡N, $-(CH_2)_{0-4}-CO-NR_{220}R_{225}$, $-(CH_2)_{0-4}-CO-(C_1-C_{12}$ alkyl), $-(CH_2)_{0-4}-CO-(C_2-C_{12}$ alkenyl), $-(CH_2)_{0-4}-CO-(C_2-C_{12}$ alkynyl), $-(CH_2)_{0-4}-CO-(C_3-C_7$ cycloalkyl), $-(CH_2)_{0-4}-CO-$aryl, $-(CH_2)_{0-4}-CO-$heteroaryl, $-(CH_2)_{0-4}-CO-$heterocyclyl, $-(CH_2)_{0-4}-CO-O-R_{215}$, $-(CH_2)_{0-4}-SO_2-NR_{220}R_{225}$, $-(CH_2)_{0-4}-SO-(C_1-C_8$ alkyl), $-(CH_2)_{0-4}-SO_2-(C_1-C_{12}$ alkyl), $-(CH_2)_{0-4}-SO_2-(C_3-C_7$ cycloalkyl), $-(CH_2)_{0-4}-N(H$ or $R_{215})-CO-O-R_{215}$, $-(CH_2)_{0-4}-N(H$ or $R_{215})-CO-N(R_{215})_2$, $-(CH_2)_{0-4}-N-CS-N(R_{215})_2$, $-(CH_2)_{0-4}-N(-H$ or $R_{215})-CO-R_{220}$, $-(CH_2)_{0-4}-NR_{220}R_{225}$, $-(CH_2)_{0-4}-O-CO-(C_1-C_6$ alkyl), $-(CH_2)_{0-4}-O-P(O)-(OR_{240})_2$, $-(CH_2)_{0-4}-O-CO-N(R_{215})_2$, $-(CH_2)_{0-4}-O-CS-N(R_{215})_2$, $-(CH_2)_{0-4}-O-(R_{215})$, $-(CH_2)_{0-4}-O-(R_{215})-COOH$, $-(CH_2)_{0-4}-S-(R_{215})$, $-(CH_2)_{0-4}-O-(C_1-C_6$ alkyl optionally substituted with 1, 2, 3,

or 5 -F), $C_3$-$C_7$ cycloalkyl, -$(CH_2)_{0-4}$-N(H or $R_{215}$)-$SO_2$-$R_{220}$, -$(CH_2)_{0-4}$- $C_3$-$C_7$ cycloalkyl, or

$C_1$-$C_{10}$ alkyl optionally substituted with 1, 2, or 3 $R_{205}$ groups, or

$C_2$-$C_{10}$ alkenyl or $C_2$-$C_{10}$ alkynyl, each of which is optionally substituted with 1 or 2 $R_{205}$ groups, wherein

the aryl and heteroaryl groups at each occurrence are optionally substituted with 1, 2, or 3 groups that are independently $R_{205}$, $R_{210}$, or

$C_1$-$C_6$ alkyl substituted with 1, 2, or 3 groups that are independently $R_{205}$ or $R_{210}$, and wherein

the heterocyclyl group at each occurrence is optionally substituted with 1, 2, or 3 groups that are independently $R_{210}$;

$R_{205}$ at each occurrence is independently selected from $C_1$-$C_6$ alkyl, halogen, -OH, -O-phenyl, -SH, -C≡N, -$CF_3$, $C_1$-$C_6$ alkoxy, $NH_2$, NH($C_1$-$C_6$ alkyl) or N-($C_1$-$C_6$ alkyl)($C_1$-$C_6$ alkyl);

$R_{210}$ at each occurrence is independently selected from halogen, $C_1$-$C_6$ alkoxy, $C_1$-$C_6$ haloalkoxy, -$NR_{220}R_{225}$, OH, C≡N, -CO-($C_1$-$C_4$ alkyl), -$SO_2$-$NR_{235}R_{240}$, -CO-$NR_{235}R_{240}$, -$SO_2$-($C_1$-$C_4$ alkyl), =O, or $C_1$-$C_6$ alkyl, $C_2$-$C_6$ alkenyl, $C_2$-$C_6$ alkynyl or $C_3$-$C_7$ cycloalkyl, each of which is optionally substituted with 1, 2, or 3 $R_{205}$ groups;

$R_{215}$ at each occurrence is independently selected from $C_1$-$C_6$ alkyl, -$(CH_2)_{0-2}$-(aryl), $C_2$-$C_6$ alkenyl, $C_2$-$C_6$ alkynyl, $C_3$-$C_7$ cycloalkyl, and -$(CH_2)_{0-2}$-(heteroaryl), -$(CH_2)_{0-2}$-(heterocyclyl), wherein

the aryl group at each occurrence is optionally substituted with 1, 2, or 3 groups that are independently $R_{205}$ or $R_{210}$, and wherein

the heterocyclyl and heteroaryl groups at each occurrence are optionally substituted with 1, 2, or 3 $R_{210}$;

$R_{220}$ and $R_{225}$ at each occurrence are independently selected from -H, $-C_3-C_7$ cycloalkyl, $-(C_1-C_2$ alkyl$)-(C_3-C_7$ cycloalkyl$)$, $-(C_1-C_6$ alkyl$)-O-(C_1-C_3$ alkyl$)$, $-C_2-C_6$ alkenyl, $-C_2-C_6$ alkynyl, $-C_1-C_6$ alkyl chain with one double bond and one triple bond, -aryl, -heteroaryl, and -heterocyclyl, or

$-C_1-C_{10}$ alkyl optionally substituted with -OH, $-NH_2$ or halogen, wherein

the aryl, heterocyclyl and heteroaryl groups at each occurrence are optionally substituted with 1, 2, or 3 $R_{270}$ groups

$R_{235}$ and $R_{240}$ at each occurrence are independently H, or $C_1-C_6$ alkyl;

$R_{245}$ and $R_{250}$ at each occurrence are independently selected from -H, $C_1-C_4$ alkyl, $C_1-C_4$ alkylaryl, $C_1-C_4$ alkylheteroaryl, $C_1-C_4$ hydroxyalkyl, $C_1-C_4$ alkoxy, $C_1-C_4$ haloalkoxy, $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl, $C_2-C_6$ alkenyl, $C_2-C_6$ alkynyl, and phenyl; or

$R_{245}$ and $R_{250}$ are taken together with the carbon to which they are attached to form a carbocycle of 3, 4, 5, 6, or 7 carbon atoms, where one carbon atom is optionally replaced by a heteroatom selected from -O-, -S-, $-SO_2-$, and $-NR_{220}-$;

$R_{255}$ and $R_{260}$ at each occurrence are independently selected from -H, $-(CH_2)_{1-2}-S(O)_{0-2}-(C_1-C_6$ alkyl$)$, $-(C_1-C_4$ alkyl$)$-aryl, $-(C_1-C_4$ alkyl$)$-heteroaryl, $-(C_1-C_4$ alkyl$)$-heterocyclyl, -aryl, -heteroaryl, -heterocyclyl, $-(CH_2)_{1-4}-R_{265}-(CH_2)_{0-4}$-aryl, $-(CH_2)_{1-4}-R_{265}-(CH_2)_{0-4}$-heteroaryl, $-(CH_2)_{1-4}-R_{265}-(CH_2)_{0-4}$-heterocyclyl, or

$C_1-C_6$ alkyl, $C_2-C_6$ alkenyl, $C_2-C_6$ alkynyl or $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl, each of which is optionally substituted with 1, 2, or 3 $R_{205}$ groups, wherein

each aryl or phenyl is optionally substituted with 1, 2, or 3 groups that are independently $R_{205}$, $R_{210}$, or

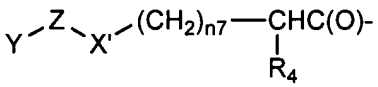
$C_1-C_6$ alkyl substituted with 1, 2, or 3 groups that are independently $R_{205}$ or $R_{210}$, and wherein

each heterocyclyl is optionally substituted with 1, 2, 3, or 4 $R_{210}$;

$R_{265}$ at each occurrence is independently -O-, -S- or -N($C_1$-$C_6$ alkyl)-;

$R_{270}$ at each occurrence is independently $R_{205}$, halogen $C_1$-$C_6$ alkoxy, $C_1$-$C_6$ haloalkoxy, $NR_{235}R_{240}$, -OH, -C≡N, -CO-($C_1$-$C_4$ alkyl), -$SO_2$-$NR_{235}R_{240}$, -CO-$NR_{235}R_{240}$, -$SO_2$-($C_1$-$C_4$ alkyl), =O, or $C_1$-$C_6$ alkyl, $C_2$-$C_6$ alkenyl, $C_2$-$C_6$ alkynyl or -$(CH_2)_{0-4}$-$C_3$-$C_7$ cycloalkyl, each of which is optionally substituted with 1, 2, or 3 $R_{205}$ groups;

$R_N$ is $R'_{100}$, -C(=O)-$NR_{100}$-$R'_{100}$, -C(=O)O-$R'_{100}$, -$SO_2R'_{100}$, -$(CRR')_{1-6}R'_{100}$, -C(=O)-$(CRR')_{0-6}R_{100}$, -C(=O)-$(CRR')_{1-6}$-O-$R'_{100}$, -C(=O)-$(CRR')_{1-6}$-S-$R'_{100}$, -C(=O)-$(CRR')_{1-6}$-C(=O)-$R_{100}$, -C(=O)-$(CRR')_{1-6}$-$SO_2$-$R_{100}$, -C(=O)-$(CRR')_{1-6}$-$NR_{100}$-$R'_{100}$, or



wherein

$R_4$ is selected from the group consisting of H; $NH_2$; -NH-$(CH_2)_{n6}$-$R_{4-1}$; -$NHR_8$; -$NR_{50}$C(O)$R_5$; $C_1$-$C_4$ alkyl-NHC(O)$R_5$; -$(CH_2)_{0-4}R_8$; -O-$C_1$-$C_4$ alkanoyl; OH; $C_6$-$C_{10}$ aryloxy optionally substituted with 1, 2, or 3 groups that are independently halogen, $C_1$-$C_4$ alkyl, -$CO_2$H, -C(O)-$C_1$-$C_4$ alkoxy, or $C_1$-$C_4$ alkoxy; $C_1$-$C_6$ alkoxy; aryl $C_1$-$C_4$ alkoxy; -$NR_{50}CO_2R_{51}$; -$C_1$-$C_4$ alkyl-$NR_{50}CO_2R_{51}$; -C≡N; -$CF_3$; -$CF_2$-$CF_3$; -C≡CH; -$CH_2$-CH=$CH_2$; -$(CH_2)_{1-4}$-$R_{4-1}$; -$(CH_2)_{1-4}$-NH-$R_{4-1}$; -O-$(CH_2)_{n6}$-$R_{4-1}$; -S-$(CH_2)_{n6}$-$R_{4-1}$; -$(CH_2)_{0-4}$-NHC(O)-$(CH_2)_{0-6}$-$R_{52}$; -$(CH_2)_{0-4}$-$R_{53}$-$(CH_2)_{0-4}$-$R_{54}$;

wherein

$n_6$ is 0, 1, 2, or 3;

$n_7$ is 0, 1, 2, or 3;

$R_{4-1}$ is selected from the group consisting of -$SO_2$-($C_1$-$C_8$ alkyl), -SO-($C_1$-$C_8$ alkyl), -S-($C_1$-$C_8$ alkyl), -S-CO-($C_1$-$C_6$ alkyl), -$SO_2$-$NR_{4-2}R_{4-3}$; -CO-$C_1$-$C_2$ alkyl; -CO-$NR_{4-3}R_{4-4}$;

$R_{4-2}$ and $R_{4-3}$ are independently H, $C_1$-$C_3$ alkyl, or $C_3$-$C_6$ cycloalkyl;

$R_{4-4}$ is alkyl, arylalkyl, alkanoyl, or arylalkanoyl;

$R_{4-6}$ is-H or $C_1$-$C_6$ alkyl;

$R_5$ is selected from the group consisting of $C_3$-$C_7$ cycloalkyl; $C_1$-$C_6$ alkyl optionally substituted with 1, 2, or 3 groups that are independently halogen, $-NR_6R_7$, $C_1$-$C_4$ alkoxy, $C_5$-$C_6$ heterocycloalkyl, $C_5$-$C_6$ heteroaryl, $C_6$-$C_{10}$ aryl, $C_3$-$C_7$ cycloalkyl $C_1$-$C_4$ alkyl, $-S$-$C_1$-$C_4$ alkyl, $-SO_2$-$C_1$-$C_4$ alkyl, $-CO_2H$, $-CONR_6R_7$, $-CO_2$-$C_1$-$C_4$ alkyl, $C_6$-$C_{10}$ aryloxy; heteroaryl optionally substituted with 1, 2, or 3 groups that are independently $C_1$-$C_4$ alkyl, $C_1$-$C_4$ alkoxy, halogen, $C_1$-$C_4$ haloalkyl, or OH; heterocycloalkyl optionally substituted with 1, 2, or 3 groups that are independently $C_1$-$C_4$ alkyl, $C_1$-$C_4$ alkoxy, halogen, or $C_2$-$C_4$ alkanoyl; aryl optionally substituted with 1, 2, 3, or 4 groups that are independently halogen, OH, $C_1$-$C_4$ alkyl, $C_1$-$C_4$ alkoxy, or $C_1$-$C_4$ haloalkyl; and $-NR_6R_7$; wherein

$R_6$ and $R_7$ are independently selected from the group consisting of H, $C_1$-$C_6$ alkyl, $C_2$-$C_6$ alkanoyl, phenyl, $-SO_2$-$C_1$-$C_4$ alkyl, phenyl $C_1$-$C_4$ alkyl;

$R_8$ is selected from the group consisting of $-SO_2$-heteroaryl, $-SO_2$-aryl, $-SO_2$-heterocycloalkyl, $-SO_2$-$C_1$-$C_{10}$ alkyl, $-C(O)NHR_9$, heterocycloalkyl, $-S$-$C_1$-$C_6$ alkyl, $-S$-$C_2$-$C_4$ alkanoyl, wherein

$R_9$ is aryl $C_1$-$C_4$ alkyl, $C_1$-$C_6$ alkyl, or H;

$R_{50}$ is H or $C_1$-$C_6$ alkyl;

$R_{51}$ is selected from the group consisting of aryl $C_1$-$C_4$ alkyl; $C_1$-$C_6$ alkyl optionally substituted with 1, 2, or 3 groups that are independently halogen, cyano, heteroaryl, $-NR_6R_7$, $-C(O)NR_6R_7$, $C_3$-$C_7$ cycloalkyl, or $-C_1$-$C_4$ alkoxy; heterocycloalkyl optionally substituted with

1 or 2 groups that are independently $C_1$-$C_4$ alkyl, $C_1$-$C_4$ alkoxy, halogen, $C_2$-$C_4$ alkanoyl, aryl $C_1$-$C_4$ alkyl, and -$SO_2$ $C_1$-$C_4$ alkyl; alkenyl; alkynyl; heteroaryl optionally substituted with 1, 2, or 3 groups that are independently OH, $C_1$-$C_4$ alkyl, $C_1$-$C_4$ alkoxy, halogen, $NH_2$, NH($C_1$-$C_6$ alkyl) or N($C_1$-$C_6$ alkyl)($C_1$-$C_6$ alkyl); heteroarylalkyl optionally substituted with 1, 2, or 3 groups that are independently $C_1$-$C_4$ alkyl, $C_1$-$C_4$ alkoxy, halogen, $NH_2$, NH($C_1$-$C_6$ alkyl) or N($C_1$-$C_6$ alkyl)($C_1$-$C_6$ alkyl); aryl; heterocycloalkyl; $C_3$-$C_8$ cycloalkyl; and cycloalkylalkyl; wherein the aryl; heterocycloalkyl, $C_3$-$C_8$ cycloalkyl, and cycloalkylalkyl groups are optionally substituted with 1, 2, 3, 4 or 5 groups that are independently halogen, CN, $NO_2$, $C_1$-$C_6$ alkyl, $C_1$-$C_6$ alkoxy, $C_2$-$C_6$ alkanoyl, $C_1$-$C_6$ haloalkyl, $C_1$-$C_6$ haloalkoxy, hydroxy, $C_1$-$C_6$ hydroxyalkyl, $C_1$-$C_6$ alkoxy $C_1$-$C_6$ alkyl, $C_1$-$C_6$ thioalkoxy, $C_1$-$C_6$ thioalkoxy $C_1$-$C_6$ alkyl, or $C_1$-$C_6$ alkoxy $C_1$-$C_6$ alkoxy;

$R_{52}$ is heterocycloalkyl, heteroaryl, aryl, cycloalkyl, -$S(O)_{0-2}$-$C_1$-$C_6$ alkyl, $CO_2H$, -C(O)$NH_2$, -C(O)NH(alkyl), -C(O)N(alkyl)(alkyl), -$CO_2$-alkyl, -NHS$(O)_{0-2}$-$C_1$-$C_6$ alkyl, -N(alkyl)S$(O)_{0-2}$-$C_1$-$C_6$ alkyl, -S$(O)_{0-2}$-heteroaryl, -S$(O)_{0-2}$-aryl, -NH(arylalkyl), -N(alkyl)(arylalkyl), thioalkoxy, or alkoxy, each of which is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently alkyl, alkoxy, thioalkoxy, halogen, haloalkyl, haloalkoxy, alkanoyl, $NO_2$, CN, alkoxycarbonyl, or aminocarbonyl;

$R_{53}$ is absent, -O-, -C(O)-, -NH-, -N(alkyl)-, -NH-S$(O)_{0-2}$-, -N(alkyl)-S$(O)_{0-2}$-, -S$(O)_{0-2}$-NH-, -S$(O)_{0-2}$- N(alkyl)-, -NH-C(S)-, or -N(alkyl)-C(S)-;

$R_{54}$ is heteroaryl, aryl, arylalkyl, heterocycloalkyl, $CO_2H$, -$CO_2$-alkyl, -C(O)NH(alkyl), -C(O)N(alkyl) (alkyl),

$-C(O)NH_2$, $C_1$-$C_8$ alkyl, OH, aryloxy, alkoxy, arylalkoxy, $NH_2$, NH(alkyl), N(alkyl) (alkyl), or $-C_1$-$C_6$ alkyl-$CO_2$-$C_1$-$C_6$ alkyl, each of which is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently alkyl, alkoxy, $CO_2H$, $-CO_2$-alkyl, thioalkoxy, halogen, haloalkyl, haloalkoxy, hydroxyalkyl, alkanoyl, $NO_2$, CN, alkoxycarbonyl, or aminocarbonyl;

X' is selected from the group consisting of $-C_1$-$C_6$ alkylidenyl optionally optionally substituted with 1, 2, or 3 methyl groups; and $-NR_{4-6}-$; or

$R_4$ and $R_{4-6}$ combine to form $-(CH_2)_{n10}-$, wherein

$n_{10}$ is 1, 2, 3, or 4;

Z is selected from the group consisting of a bond; $SO_2$; SO; S; and C(O);

Y is selected from the group consisting of H; $C_1$-$C_4$ haloalkyl; $C_5$-$C_6$ heterocycloalkyl; $C_6$-$C_{10}$ aryl; OH; $-N(Y_1)(Y_2)$; $C_1$-$C_{10}$ alkyl optionally substituted with 1 thru 3 substituents which can be the same or different and are selected from the group consisting of halogen, hydroxy, alkoxy, thioalkoxy, and haloalkoxy; $C_3$-$C_8$ cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from $C_1$-$C_3$ alkyl, and halogen; alkoxy; aryl optionally substituted with halogen, alkyl, alkoxy, CN or $NO_2$; arylalkyl optionally substituted with halogen, alkyl, alkoxy, CN or $NO_2$; wherein

$Y_1$ and $Y_2$ are the same or different and are H; $C_1$-$C_{10}$ alkyl optionally substituted with 1, 2, or 3 substituents selected from the group consisting of halogen, $C_1$-$C_4$ alkoxy, $C_3$-$C_8$ cycloalkyl, and OH; $C_2$-$C_6$ alkenyl; $C_2$-$C_6$ alkanoyl; phenyl; $-SO_2$-$C_1$-$C_4$ alkyl; phenyl $C_1$-$C_4$ alkyl; or $C_3$-$C_8$ cycloalkyl $C_1$-$C_4$ alkyl; or

$Y_1$, $Y_2$ and the nitrogen to which they are attached form a ring selected from the group consisting of piperazinyl, piperidinyl, morpholinyl, and pyrolidinyl, wherein each

ring is optionally substituted with 1, 2, 3, or 4 groups that are independently $C_1$-$C_6$ alkyl, $C_1$-$C_6$ alkoxy, $C_1$-$C_6$ alkoxy $C_1$-$C_6$ alkyl, or halogen;

$R_{100}$ and $R'_{100}$ independently represent aryl, heteroaryl, -aryl-W-aryl, -aryl-W-heteroaryl, -aryl-W-heterocyclyl, -heteroaryl-W-aryl, -heteroaryl-W-heteroaryl, -heteroaryl-W-heterocyclyl, -heterocyclyl-W-aryl, -heterocyclyl-W-heteroaryl, -heterocyclyl-W-heterocyclyl, $-CH[(CH_2)_{0-2}-O-R_{150}]-(CH_2)_{0-2}$-aryl, $-CH[(CH_2)_{0-2}-O-R_{150}]-(CH_2)_{0-2}$-heterocyclyl or $-CH[(CH_2)_{0-2}-O-R_{150}]-(CH_2)_{0-2}$-heteroaryl, where the ring portions of each are optionally substituted with 1, 2, or 3 groups independently selected from

-OR, $-NO_2$, halogen, $-C\equiv N$, $-OCF_3$, $-CF_3$, $-(CH_2)_{0-4}-O-P(=O)(OR)(OR')$, $-(CH_2)_{0-4}-CO-NR_{105}R'_{105}$, $-(CH_2)_{0-4}-O-(CH_2)_{0-4}-CONR_{102}R_{102}'$, $-(CH_2)_{0-4}-CO-(C_1-C_{12}$ alkyl), $-(CH_2)_{0-4}-CO-(C_2-C_{12}$ alkenyl), $-(CH_2)_{0-4}-CO-(C_2-C_{12}$ alkynyl), $-(CH_2)_{0-4}-CO-(CH_2)_{0-4}(C_3-C_7$ cycloalkyl), $-(CH_2)_{0-4}-R_{110}$, $-(CH_2)_{0-4}-R_{120}$, $-(CH_2)_{0-4}-R_{130}$, $-(CH_2)_{0-4}-CO-R_{110}$, $-(CH_2)_{0-4}-CO-R_{120}$, $-(CH_2)_{0-4}-CO-R_{130}$, $-(CH_2)_{0-4}-CO-R_{140}$, $-(CH_2)_{0-4}-CO-O-R_{150}$, $-(CH_2)_{0-4}-SO_2-NR_{105}R'_{105}$, $-(CH_2)_{0-4}-SO-(C_1-C_8$ alkyl), $-(CH_2)_{0-4}-SO_2-(C_1-C_{12}$ alkyl), $-(CH_2)_{0-4}-SO_2-(CH_2)_{0-4}-(C_3-C_7$ cycloalkyl), $-(CH_2)_{0-4}-N(R_{150})-CO-O-R_{150}$, $-(CH_2)_{0-4}-N(R_{150})-CO-N(R_{150})_2$, $-(CH_2)_{0-4}-N(R_{150})-CS-N(R_{150})_2$, $-(CH_2)_{0-4}-N(R_{150})-CO-R_{105}$, $-(CH_2)_{0-4}-NR_{105}R'_{105}$, $-(CH_2)_{0-4}-R_{140}$, $-(CH_2)_{0-4}-O-CO-(C_1-C_6$ alkyl), $-(CH_2)_{0-4}-O-P(O)-(O-R_{110})_2$, $-(CH_2)_{0-4}-O-CO-N(R_{150})_2$, $-(CH_2)_{0-4}-O-CS-N(R_{150})_2$, $-(CH_2)_{0-4}-O-(R_{150})$, $-(CH_2)_{0-4}-O-R_{150}'-COOH$, $-(CH_2)_{0-4}-S-(R_{150})$, $-(CH_2)_{0-4}-N(R_{150})-SO_2-R_{105}$, $-(CH_2)_{0-4}-$ $C_3-C_7$ cycloalkyl, $(C_2-C_{10})$alkenyl, or $(C_2-C_{10})$alkynyl, or

$R_{100}$ is $C_1-C_{10}$ alkyl optionally substituted with 1, 2, or 3 $R_{115}$ groups, or

$R_{100}$ is $-(C_1-C_6$ alkyl$)-O-C_1-C_6$ alkyl) or $-(C_1-C_6$ alkyl$)-S-(C_1-C_6$ alkyl), each of which is optionally substituted with 1, 2, or 3 $R_{115}$ groups, or

$R_{100}$ is $C_3-C_8$ cycloalkyl optionally substituted with 1, 2, or 3 $R_{115}$ groups;

W is $-(CH_2)_{0-4}-$, $-O-$, $-S(O)_{0-2}-$, $-N(R_{135})-$, $-CR(OH)-$ or $-C(O)-$;

$R_{102}$ and $R_{102}'$ independently are hydrogen, or

$C_1-C_{10}$ alkyl optionally substituted with 1, 2, or 3 groups that are independently halogen, aryl or $-R_{110}$;

$R_{105}$ and $R'_{105}$ independently represent $-H$, $-R_{110}$, $-R_{120}$, $C_3-C_7$ cycloalkyl, $-(C_1-C_2$ alkyl$)-(C_3-C_7$ cycloalkyl), $-(C_1-C_6$ alkyl$)-O-(C_1-C_3$ alkyl), $C_2-C_6$ alkenyl, $C_2-C_6$ alkynyl, or $C_1-C_6$ alkyl chain with one double bond and one triple bond, or

$C_1-C_6$ alkyl optionally substituted with $-OH$ or $-NH_2$; or,

$C_1-C_6$ alkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, or

$R_{105}$ and $R'_{105}$ together with the atom to which they are attached form a 3 to 7 membered carbocylic ring, where one member is optionally a heteratom selected from $-O-$, $-S(O)_{0-2}-$, $-N(R_{135})-$, the ring being optionally substituted with 1, 2 or three $R_{140}$ groups;

$R_{115}$ at each occurrence is independently halogen, $-OH$, $-CO_2R_{102}$, $-C_1-C_6$ thioalkoxy, $-CO_2-$phenyl, $-NR_{105}R'_{135}$, $-SO_2-(C_1-C_8$ alkyl), $-C(=O)R_{180}$, $R_{180}$, $-CONR_{105}R'_{105}$, $-SO_2NR_{105}R'_{105}$, $-NH-CO-(C_1-C_6$ alkyl), $-NH-C(=O)-OH$, $-NH-C(=O)-OR$, $-NH-C(=O)-O-$phenyl, $-O-C(=O)-(C_1-C_6$ alkyl), $-O-C(=O)-$amino, $-O-C(=O)-$mono- or dialkylamino, $-O-C(=O)-$phenyl, $-O-(C_1-C_6$ alkyl$)-CO_2H$, $-NH-SO_2-(C_1-C_6$ alkyl), $C_1-C_6$ alkoxy or $C_1-C_6$ haloalkoxy;

$R_{135}$ is $C_1-C_6$ alkyl, $C_2-C_6$ alkenyl, $C_2-C_6$ alkynyl, $C_3-C_7$ cycloalkyl, $-(CH_2)_{0-2}-$(aryl), $-(CH_2)_{0-2}-$(heteroaryl), or $-(CH_2)_{0-2}-$(heterocyclyl);

$R_{140}$ is heterocyclyl optionally substituted with 1, 2, 3, or 4 groups independently selected from $C_1-C_6$ alkyl, $C_1-C_6$ alkoxy,

halogen, hydroxy, cyano, nitro, amino, mono($C_1$-$C_6$)alkylamino, di($C_1$-$C_6$)alkylamino, $C_2$-$C_6$ alkenyl, $C_2$-$C_6$ alkynyl, $C_1$-$C_6$ haloalkyl, $C_1$-$C_6$ haloalkoxy, amino($C_1$-$C_6$)alkyl, mono($C_1$-$C_6$)alkylamino($C_1$-$C_6$)alkyl, di($C_1$-$C_6$)alkylamino($C_1$-$C_6$)alkyl, and =O;

$R_{150}$ is hydrogen, $C_3$-$C_7$ cycloalkyl, -($C_1$-$C_2$ alkyl)-($C_3$-$C_7$ cycloalkyl), $C_2$-$C_6$ alkenyl, $C_2$-$C_6$ alkynyl, $C_1$-$C_6$ alkyl with one double bond and one triple bond, -$R_{110}$, -$R_{120}$, or

$C_1$-$C_6$ alkyl optionally substituted with 1, 2, 3, or 4 groups independently selected from -OH, -$NH_2$, $C_1$-$C_3$ alkoxy, $R_{110}$, and halogen;

$R_{150}'$ is $C_3$-$C_7$ cycloalkyl, -($C_1$-$C_3$ alkyl)-($C_3$-$C_7$ cycloalkyl), $C_2$-$C_6$ alkenyl, $C_2$-$C_6$ alkynyl, $C_1$-$C_6$ alkyl with one double bond and one triple bond, -$R_{110}$, -$R_{120}$, or

$C_1$-$C_6$ alkyl optionally substituted with 1, 2, 3, or 4 groups independently selected from -OH, -$NH_2$, $C_1$-$C_3$ alkoxy, $R_{110}$, and halogen;

$R_{180}$ is selected from morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl, homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S-oxide, homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl, each of which is optionally substituted with 1, 2, 3, or 4 groups independently selected from $C_1$-$C_6$ alkyl, $C_1$-$C_6$ alkoxy, halogen, hydroxy, cyano, nitro, amino, mono($C_1$-$C_6$)alkylamino, di($C_1$-$C_6$)alkylamino, $C_2$-$C_6$ alkenyl, $C_2$-$C_6$ alkynyl, $C_1$-$C_6$ haloalkyl, $C_1$-$C_6$ haloalkoxy, amino($C_1$-$C_6$)alkyl, mono($C_1$-$C_6$)alkylamino($C_1$-$C_6$)alkyl, di($C_1$-$C_6$)alkylamino($C_1$-$C_6$)alkyl, and =O;

$R_{110}$ is aryl optionally substituted with 1 or 2 $R_{125}$ groups;

$R_{125}$ at each occurrence is independently halogen, amino, mono- or dialkylamino, -OH, -C≡N, -$SO_2$-$NH_2$, -$SO_2$-NH-$C_1$-$C_6$ alkyl, -$SO_2$-N($C_1$-$C_6$ alkyl)$_2$, -$SO_2$-($C_1$-$C_4$ alkyl), -CO-$NH_2$, -CO-NH-$C_1$-$C_6$ alkyl, or -CO-N($C_1$-$C_6$ alkyl)$_2$, or

$C_1$-$C_6$ alkyl, $C_2$-$C_6$ alkenyl or $C_2$-$C_6$ alkynyl, each of which is optionally substituted with 1, 2, or 3 groups that are independently selected from $C_1$-$C_3$ alkyl, halogen, -OH, -SH, -C≡N, $-CF_3$, $C_1$-$C_3$ alkoxy, amino, and mono- and dialkylamino, or

$C_1$-$C_6$ alkoxy optionally substituted with one, two or three of halogen;

$R_{120}$ is heteroaryl, which is optionally substituted with 1 or 2 $R_{125}$ groups; and

$R_{130}$ is heterocyclyl optionally substituted with 1 or 2 $R_{125}$ groups; and

$R_2$ is selected from the group consisting of H; $C_1$-$C_6$ alkyl, optionally substituted with 1, 2, or 3 substituents that are independently selected from the group consisting of $C_1$-$C_3$ alkyl, halogen, -OH, -SH, -C≡N, $-CF_3$, $C_1$-$C_3$ alkoxy, and $-NR_{1-a}R_{1-b}$; wherein

$R_{1-a}$ and $R_{1-b}$ are -H or $C_1$-$C_6$ alkyl;
$-(CH_2)_{0-4}$-aryl; $-(CH_2)_{0-4}$-heteroaryl; $C_2$-$C_6$ alkenyl; $C_2$-$C_6$ alkynyl; $-CONR_{N-2}R_{N-3}$; $-SO_2NR_{N-2}R_{N-3}$; $-CO_2H$; and $-CO_2-(C_1$-$C_4$ alkyl);

$R_3$ is selected from the group consisting of H; $C_1$-$C_6$ alkyl, optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of $c_1$-$c_3$ alkyl, halogen, -OH, -SH, -C≡N, $-CF_3$, $C_1$-$C_3$ alkoxy, and $-NR_{1-a}R_{1-b}$; $-(CH_2)_{0-4}$-aryl; $-(CH_2)_{0-4}$-heteroaryl; $C_2$-$C_6$ alkenyl; $C_2$-$C_6$ alkynyl; $-CO-NR_{n-2}R_{n-3}$; $-SO_2-NR_{n-2}R_{n-3}$; $-CO_2H$; and - CO-O-($C_1$-$C_4$ alkyl);

wherein

$R_{N-2}$ and $R_{N-3}$ at each occurrence are independently selected from the group consisting of $-C_1$-$C_8$ alkyl optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of -

OH, $-NH_2$, phenyl and halogen; $-C_3-C_8$ cycloalkyl; $-(C_1-C_2$ alkyl$)-(C_3-C_8$ cycloalkyl); $-(C_1-C_6$ alkyl$)-O-(C_1-C_3$ alkyl); $-C_2-C_6$ alkenyl; $-C_2-C_6$ alkynyl; $-C_1-C_6$ alkyl chain with one double bond and one triple bond; aryl; heteroaryl; heterocycloalkyl; or

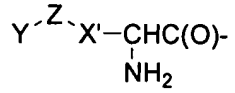
$R_{N-2}$, $R_{N-3}$ and the nitrogen to which they are attached form a 5, 6, or 7 membered heterocycloalkyl or heteroaryl group, wherein said heterocycloalkyl or heteroaryl group is optionally fused to a benzene, pyridine, or pyrimidine ring, and said groups are unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that at each occurrence are independently $C_1-C_6$ alkyl, $C_1-C_6$ alkoxy, halogen, halo $C_1-C_6$ alkyl, halo $C_1-C_6$ alkoxy, $-CN$, $-NO_2$, $-NH_2$, $NH(C_1-C_6$ alkyl), $N(C_1-C_6$ alkyl$)(C_1-C_6$ alkyl), $-OH$, $-C(O)NH_2$, $-C(O)NH(C_1-C_6$ alkyl), $-C(O)N(C_1-C_6$ alkyl$)(C_1-C_6$ alkyl), $C_1-C_6$ alkoxy $C_1-C_6$ alkyl, $C_1-C_6$ thioalkoxy, and $C_1-C_6$ thioalkoxy $C_1-C_6$ alkyl;

or wherein,

$R_2$, $R_3$ and the carbon to which they are attached form a carbocycle of three thru seven carbon atoms, wherein one carbon atom is optionally replaced by a group selected from-O-, -S-, -$SO_2$-, or $-NR_{N-2}$-.

Claim 2. (original) A compound according to claim 1 wherein RN is $R_N$ is $R'_{100}$, $-C(=O)-NR_{100}-R'_{100}$, $-C(=O)O-R'_{100}$, $-SO_2R'_{100}$, $-(CRR')_{1-6}R'_{100}$, $-C(=O)-(CRR')_{0-6}R_{100}$, $-C(=O)-(CRR')_{1-6}-O-R'_{100}$, $-C(=O)-(CRR')_{1-6}-S-R'_{100}$, $-C(=O)-(CRR')_{1-6}-C(=O)-R_{100}$, $-C(=O)-(CRR')_{1-6}-SO_2-R_{100}$, or $-C(=O)-(CRR')_{1-6}-NR_{100}-R'_{100}$.

Claim 3. (original) A compound according to claim 1, wherein $R_N$ is



wherein

X′ is $C_1$-$C_4$ alkylidenyl optionally substituted with 1, 2, or 3 methyl groups; or $-NR_{4-6}-$, where $R_{4-6}$ is–H or $C_1$-$C_6$ alkyl; or

$R_4$ and $R_{4-6}$ combine to form $-(CH_2)_{n10}-$, wherein

$n_{10}$ is 1, 2, 3, or 4;

Z is selected from a bond; $SO_2$; SO; S; and C(O);

Y is selected from H; $C_1$-$C_4$ haloalkyl; $C_5$-$C_6$ heterocycloalkyl containing at least one N, O, or S; phenyl; OH; $-N(Y_1)(Y_2)$; $C_1$-$C_{10}$ alkyl optionally substituted with 1 thru 3 substituents which can be the same or different and are selected from halogen, hydroxy, alkoxy, thioalkoxy, and haloalkoxy; $C_3$-$C_8$ cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from $C_1$-$C_3$ alkyl, and halogen; alkoxy; phenyl optionally substituted with halogen, $C_1$-$C_4$ alkyl, $C_1$-$C_4$ alkoxy, CN or $NO_2$; phenyl $C_1$-$C_4$ alkyl optionally substituted with halogen, $C_1$-$C_4$ alkyl, $C_1$-$C_4$ alkoxy, CN or $NO_2$; wherein

$Y_1$ and $Y_2$ are the same or different and are H; $C_1$-$C_{10}$ alkyl optionally substituted with 1, 2, or 3 substituents selected from the group consisting of halogen, $C_1$-$C_4$ alkoxy, $C_3$-$C_8$ cycloalkyl, and OH; $C_2$-$C_6$ alkenyl; $C_2$-$C_6$ alkanoyl; phenyl; $-SO_2$-$C_1$-$C_4$ alkyl; phenyl $C_1$-$C_4$ alkyl; and $C_3$-$C_8$ cycloalkyl $C_1$-$C_4$ alkyl; or $-N(Y_1)(Y_2)$ forms a ring selected from piperazinyl, piperidinyl, morpholinyl, and pyrolidinyl, wherein each ring is optionally substituted with 1, 2, 3, or 4 groups that are independently $C_1$-$C_6$ alkyl, $C_1$-$C_6$ alkoxy, $C_1$-$C_6$ alkoxy $C_1$-$C_6$ alkyl, or halogen.

Claim 4. (original) A compound according to claim 1, wherein $R_1$ is aryl, heteroaryl, heterocyclyl, -$C_1$-$C_6$ alkyl-aryl, -

$C_1$-$C_6$ alkyl-heteroaryl, or -$C_1$-$C_6$ alkyl-heterocyclyl, where the ring portions of each are optionally substituted with 1, 2, 3, or 4 groups independently selected from halogen, -OH, -SH, -C≡N, -$NO_2$, -$NR_{105}R'_{105}$, -$CO_2R$, -N(R)COR', or -N(R)$SO_2$R' (where $R_{105}$, $R'_{105}$, R and R' are as defined above), -C(=O)-($C_1$-$C_4$) alkyl, -$SO_2$-amino, -$SO_2$-mono or dialkylamino, -C(=O)-amino, -C(=O)-mono or dialkylamino, -$SO_2$-($C_1$-$C_4$) alkyl, or

$C_1$-$C_6$ alkoxy optionally substituted with 1, 2, or 3 groups which are independently selected from halogen, or

$C_3$-$C_7$ cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, -SH, -C≡N, -$CF_3$, $C_1$-$C_3$ alkoxy, amino, -$C_1$-$C_6$ alkyl and mono- or dialkylamino, or

$C_1$-$C_{10}$ alkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, -SH, -C≡N, -$CF_3$, -$C_1$-$C_3$ alkoxy, amino, mono- or dialkylamino and -$C_1$-$C_3$ alkyl, or

$C_2$-$C_{10}$ alkenyl or $C_2$-$C_{10}$ alkynyl each of which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, -SH, -C≡N, -$CF_3$, $C_1$-$C_3$ alkoxy, amino, $C_1$-$C_6$ alkyl and mono- or dialkylamino; and the heterocyclyl group is optionally further substituted with oxo.

Claim 5. (original) A compound according to claim 4, wherein $R_1$ is

-$C_1$-$C_6$ alkyl-aryl, -$C_1$-$C_6$ alkyl-heteroaryl, or -$C_1$-$C_6$ alkyl-heterocyclyl, where the ring portions of each are optionally substituted with 1, 2, 3, or 4 groups independently selected from halogen, -OH, -SH, -C≡N, -$NO_2$, -$NR_{105}R'_{105}$, -$CO_2R$, -N(R)COR', or -N(R)$SO_2$R' (where $R_{105}$, $R'_{105}$, R and R' are as defined above),

$-C(=O)-(C_1-C_4)$ alkyl, $-SO_2$-amino, $-SO_2$-mono or dialkylamino, $-C(=O)$-amino, $-C(=O)$-mono or dialkylamino, $-SO_2-(C_1-C_4)$ alkyl, or

$C_1-C_6$ alkoxy optionally substituted with 1, 2, or 3 groups which are independently selected from halogen, or

$C_3-C_7$ cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, -SH, $-C\equiv N$, $-CF_3$, $C_1-C_3$ alkoxy, amino, $-C_1-C_6$ alkyl and mono- or dialkylamino, or

$C_1-C_{10}$ alkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, -SH, $-C\equiv N$, $-CF_3$, $-C_1-C_3$ alkoxy, amino, mono- or dialkylamino and $-C_1-C_3$ alkyl, or

$C_2-C_{10}$ alkenyl or $C_2-C_{10}$ alkynyl each of which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, -SH, $-C\equiv N$, $-CF_3$, $C_1-C_3$ alkoxy, amino, $C_1-C_6$ alkyl and mono- or dialkylamino; and the heterocyclyl group is optionally further substituted with oxo.

Claim 6. (original) A compound according to claim 1 wherein:

$R_N$ is $-C(=O)-R_{100}$; and

$R_{100}$ represents aryl, or heteroaryl, where the ring portions of each are optionally substituted with 1, 2, or 3 groups independently selected from

-OR, $-NO_2$, $C_1-C_6$ alkyl, halogen, $-C\equiv N$, $-OCF_3$, $-CF_3$, $-(CH_2)_{0-4}-O-P(=O)(OR)(OR')$, $-(CH_2)_{0-4}-CO-NR_{105}R'_{105}$, $-(CH_2)_{0-4}-O-(CH_2)_{0-4}-CONR_{102}R_{102}'$, $-(CH_2)_{0-4}-CO-(C_1-C_{12}$ alkyl), $-(CH_2)_{0-4}-CO-(C_2-C_{12}$ alkenyl), $-(CH_2)_{0-4}-CO-(C_2-C_{12}$ alkynyl), $-(CH_2)_{0-4}-CO-(CH_2)_{0-4}(C_3-C_7$ cycloalkyl), $-(CH_2)_{0-4}-R_{110}$, $-(CH_2)_{0-4}-R_{120}$, $-(CH_2)_{0-4}-R_{130}$, $-(CH_2)_{0-4}-CO-R_{110}$, $-(CH_2)_{0-4}-CO-R_{120}$, $-(CH_2)_{0-4}-CO-R_{130}$, $-(CH_2)_{0-4}-CO-R_{140}$, $-(CH_2)_{0-4}-CO-O-R_{150}$, $-(CH_2)_{0-4}-SO_2-NR_{105}R'_{105}$, $-(CH_2)_{0-4}-SO-(C_1-C_8$ alkyl), $-(CH_2)_{0-4}-SO_2-(C_1-C_{12}$ alkyl), $-(CH_2)_{0-4}-SO_2-(CH_2)_{0-4}-(C_3-C_7$ cycloalkyl), $-(CH_2)_{0-4}-N(R_{150})-CO-O-R_{150}$, $-(CH_2)_{0-4}-N(R_{150})-$

$CO-N(R_{150})_2$, $-(CH_2)_{0-4}-N(R_{150})-CS-N(R_{150})_2$, $-(CH_2)_{0-4}-N(R_{150})-CO-R_{105}$, $-(CH_2)_{0-4}-NR_{105}R'_{105}$, $-(CH_2)_{0-4}-R_{140}$, $-(CH_2)_{0-4}-O-CO-(C_1-C_6$ alkyl), $-(CH_2)_{0-4}-O-P(O)-(O-R_{110})_2$, $-(CH_2)_{0-4}-O-CO-N(R_{150})_2$, $-(CH_2)_{0-4}-O-CS-N(R_{150})_2$, $-(CH_2)_{0-4}-O-(R_{150})$, $-(CH_2)_{0-4}-O-R_{150}'-COOH$, $-(CH_2)_{0-4}-S-(R_{150})$, $-(CH_2)_{0-4}-N(R_{150})-SO_2-R_{105}$, $-(CH_2)_{0-4}-$ $C_3-C_7$ cycloalkyl, $(C_2-C_{10})$alkenyl, or $(C_2-C_{10})$alkynyl.

Claim 7. (original) A compound according to claim 1 wherein:

$R_C$ is hydrogen, $-(CR_{245}R_{250})_{0-4}$-aryl, $-(CR_{245}R_{250})_{0-4}$-heteroaryl, $-(CR_{245}R_{250})_{0-4}$-heterocyclyl,

$C_2-C_{10}$ alkyl optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of $R_{205}$, $R_{110}$, $R_{120}$, $R_{130}$, $-OC=ONR_{235}R_{240}$, $-S(=O)_{0-2}(C_1-C_6$ alkyl), -SH, and $-S(=O)_2NR_{235}R_{240}$,

$-(CH_2)_{0-3}-(C_3-C_8)$ cycloalkyl wherein the cycloalkyl is optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of $R_{205}$, $-CO_2H$, and $-CO_2-(C_1-C_4$ alkyl), or

$C_2-C_{10}$ alkenyl or $C_2-C_{10}$ alkynyl, each of which is optionally substituted with 1, 2, or 3 independently selected $R_{205}$ groups, wherein

each aryl and heteroaryl is optionally substituted with 1, 2, or 3 $R_{200}$, and wherein each heterocyclyl is optionally substituted with 1, 2, 3, or 4 independently selected $R_{210}$ groups.

Claim 8. (original) A compound according to claim 1 wherein $R_2$, $R_3$, and $R_{20}$ are each hydrogen.

Claim 9. (currently amended) A compound according to claim 1 selected from the group consisting of:

N-(3,5-difluorobenzyl)-N-{(2R)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methyl-N',N'-dipropylisophthalamide;

N-[2-(3,5-difluorophenyl)ethyl]-N-{(2R)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methyl-N',N'-dipropylisophthalamide;

3-[([2-(3,5-difluorophenyl)ethyl]{(2R)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}amino)sulfonyl]-N,N-dipropylbenzamide;

*N*-(3,5-difluorobenzyl)-*N*-((2*R*)-3-{[(4*R*)-6-ethyl-2,2-dioxido-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}-2-hydroxypropyl)-5-methyl-*N*',*N*'-dipropylisophthalamide;

*N*-[2-(3,5-difluorophenyl)ethyl]-*N*-((2*R*)-3-{[(4*R*)-6-ethyl-2,2-dioxido-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}-2-hydroxypropyl)-5-methyl-*N*',*N*'-dipropylisophthalamide;

3-{[[2-(3,5-difluorophenyl)ethyl]((2*R*)-3-{[(4*R*)-6-ethyl-2,2-dioxido-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}-2-hydroxypropyl)amino]sulfonyl}-*N*,*N*-dipropylbenzamide;

*N*-(3,5-difluorobenzyl)-*N*-{(2*R*)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-*N*',*N*',5-trimethylisophthalamide;

*N*-[2-(3,5-difluorophenyl)ethyl]-*N*-{(2*R*)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-*N*',*N*',5-trimethylisophthalamide;

3-[([2-(3,5-difluorophenyl)ethyl]{(2*R*)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}amino)sulfonyl]-*N*,*N*-dimethylbenzamide;

*N*-(3,5-difluorobenzyl)-*N*-((2*R*)-3-{[(4*R*)-6-ethyl-2,2-dioxido-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}-2-hydroxypropyl)-*N*',*N*',5-trimethylisophthalamide;

*N*-[2-(3,5-difluorophenyl)ethyl]-*N*-((2*R*)-3-{[(4*R*)-6-ethyl-2,2-dioxido-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}-2-hydroxypropyl)-*N*',*N*',5-trimethylisophthalamide;

3-{[[2-(3,5-difluorophenyl)ethyl]((2*R*)-3-{[(4*R*)-6-ethyl-2,2-dioxido-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}-2-hydroxypropyl)amino]sulfonyl}-*N*,*N*-dimethylbenzamide;

*N*-(3-chloro-5-fluorobenzyl)-*N*-{(2*R*)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methyl-*N*',*N*'-dipropylisophthalamide;

*N*-[2-(3-chloro-5-fluorophenyl)ethyl]-*N*-{(2*R*)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methyl-*N*',*N*'-dipropylisophthalamide;

3-[([2-(3-chloro-5-fluorophenyl)ethyl]{(2*R*)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}amino)sulfonyl]-*N*,*N*-dipropylbenzamide;

*N*-(3-chloro-5-fluorobenzyl)-*N*-((2*R*)-3-{[(4*R*)-6-ethyl-2,2-dioxido-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}-2-hydroxypropyl)-5-methyl-*N*',*N*'-dipropylisophthalamide;

*N*-[2-(3-chloro-5-fluorophenyl)ethyl]-*N*-((2*R*)-3-{[(4*R*)-6-ethyl-2,2-dioxido-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}-2-hydroxypropyl)-5-methyl-*N*',*N*'-dipropylisophthalamide;

3-{[[2-(3-chloro-5-fluorophenyl)ethyl]((2*R*)-3-{[(4*R*)-6-ethyl-2,2-dioxido-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}-2-hydroxypropyl)amino]sulfonyl}-*N*,*N*-dipropylbenzamide;

*N*-[(2*R*)-3-(benzylamino)-2-hydroxypropyl]-*N*-(3,5-difluorobenzyl)-5-methyl-*N*',*N*'-dipropylisophthalamide;

*N*-[(2*R*)-3-(benzylamino)-2-hydroxypropyl]-*N*-[2-

(3,5-difluorophenyl)ethyl]-5-methyl-*N'*,*N'*-dipropylisophthalamide; ~~and~~

3-({[(2*R*)-3-(benzylamino)-2-hydroxypropyl][2-(3,5-difluorophenyl)ethyl]amino}sulfonyl)-*N*,*N*-dipropylbenzamide;

and salts therof.

Claim 10. (currently amended) A pharmaceutical composition comprising a compound according to claim 1 ~~any one of claims 1-9~~, in combination with a physiologically acceptable carrier or excipient.

Claims 11-12. (cancelled)

Claim 13. (original) A method for treating a patient who has, or in preventing a patient from getting, a disease or condition selected from the group consisting of Alzheimer's disease, for helping prevent or delay the onset of Alzheimer's disease, for treating patients with mild cognitive impairment (MCI) and preventing or delaying the onset of Alzheimer's disease in those who would progress from MCI to AD, for treating Down's syndrome, for treating humans who have Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type, for treating cerebral amyloid angiopathy and preventing its potential consequences, i.e. single and recurrent lobar hemorrhages, for treating other degenerative dementias, including dementias of mixed vascular and degenerative origin, dementia associated with Parkinson's disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration, or diffuse Lewy body type of Alzheimer's disease and who is in need of such treatment, comprising administering to such patient a therapeutically effective amount of a compound of claim 1.

Claim 14. (original) A method for the treatment or prevention of Alzheimer's disease, mild cognitive impairment Down's syndrome, Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type, cerebral amyloid angiopathy, other degenerative dementias, dementias of mixed vascular and degenerative origin, dementia associated with Parkinson's disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration, diffuse Lewy body type of Alzheimer's disease comprising administration of a therapeutically effective amount of a compound or salt according to Claim 1, to a patient in need thereof.

Claim 15. (original) A method for making a compound of claim 1.